## REMARKS

Claims 4-9 and 12-16 are pending in this application. Claims 12 and 13 have been amended herein. No new matter had been added by this amendment.

The amendments to claims 12 and 13 are for clarity, and are discussed below in regard to the rejection under 35 U.S.C.112, second paragraph.

**Claims 4-5, 7-9 and 12-16 are rejected under 35 U.S.C. §103(a) as being unpatentable over Hamad et al. (Journal of Applied Microbiology, 1997, Vol. 83, 764-770), in view of Wilding et al. (5,498,392).** (Office action paragraph no. 8)

The rejection of claims 4-5, 7-9 and 12-16, is respectfully traversed.

Applicants note that this rejection represents a repetition of the rejection made in the Office action dated September 24, 2003. Applicants traversed the rejection in the Response dated December 18, 2003, which was not entered. Applicants here repeat the arguments from the Response of December 18, 2003, and also address the issues raised by the Examiner in the Advisory action mailed January 14, 2004.

Arguments previously made on December 18, 2003.

The Examiner cites Hamad's method of studying microflora of Sudanese sorghum flour as disclosing the elements of the claims except for the detector in which a probe is arranged on specific positions. Wilding is cited for the disclosure of such a detector.

In the Amendment of July 10, 2003, Applicants argued that the claims require "amplifying

nucleic acid of an intestinal bacterial group ...", and that Hamad does not disclose or suggest this. This argument is relevant to all of claims 4, 5, 7-9 and 12-16. The Examiner responds to this argument on page 4, line 11, of the final Office action, by arguing that Hamad et al. discloses the study of *E. faecalis*, which the Examiner considers to be an intestinal bacterial flora.

In response, Applicants argue that "intestinal bacterial group" refers to the group of bacteria from an intestinal sample, not merely a bacterium which can be found in an intestine. The Examiner states on page 4, lines 15-20, that the disclosure of Hamad et al. would motivate one of skill in the art to analyze intestinal bacterial flora from a subject. The gist of the Examiner's argument, however, appears to be that the motivation arises because it would be **possible** due to the similarity in the 16S rRNA. Applicants submit that this does not actually provide a **motivation** for the modification of the reference to have the "intestinal bacterial flora" limitation, but only an indication of reasonable expectation of success.

Applicants also argued in the Amendment that there is no teaching or suggestion in Hamad et al. or Wilding et al. for rapid simultaneous detection of a plurality of (strains of) bacteria, as is implied by the recitation of "intestinal bacterial group" in claim 5. The Examiner addresses these arguments on page 5, lines 5-14 of the final Office action. The Examiner states that Hamad et al. "was applied to detect a plurality of bacteria since the Sorghum flour contained more than one bacteria", citing page 765, column 2, first and second paragraphs.

Applicants respectfully disagree with the Examiner's reasoning. The fact that Hamad is studying different bacteria in the sorghum flour does not mean that Hamad is providing **rapid**

**simultaneous detection** of these bacteria, and in particular Hamad et al. does not analyze based on the presence or absence of hybridization with a plurality of probes as recited in claim 5.

The Examiner cites Wilding et al. as disclosing a plurality of detection/reaction chambers to enable the rapid parallel detection of polynucleotides in a mixture, citing column 5, lines 9-11. In response, Applicants argue that even if Wilding's device were capable of performing the method of claim 5, Wilding, too, fails to provide a motivation for analyzing an intestinal bacterial group as recited in claim 5.

Moreover, even if Hamad et al. did suggest study of an intestinal bacterial group with a plurality of probes, this analysis could not be conducted in a single device of Wilding's. In the Wilding et al. device, there is no disclosure or suggestion of use of a plurality of probes, in particular where such probes are arranged on specific positions in a detector. It is not clear that the disclosure of Wilding et al. enables such a device.

Therefore, use of Wilding's devices for this purpose would require use of multiple devices, one for each probe. This, however, would be inconsistent with the recitation of claim 5, in which "said probes are arranged on specific positions on a detector."

Applicants therefore submit that claims 4, 5, 7-9 and 12-16 are novel and non-obvious over Hamad et al. and Wilding et al., taken separately or in combination.

Additional comments including comments in response to remarks in the Advisory Action mailed January 14. 2003.

In response to Applicants' arguments that the Examiner's previous arguments did not provide a **motivation** for the modification of the reference, only an indication of reasonable expectation of success, the Examiner stated in the Advisory Action:

> "The indication of reasonable motivation of success is a motivation to apply the method of Hamad to analyzing an intestinal bacterial flora."

Applicants respectfully submit that this is incorrect, noting that MPEP 2142 provides:

> "To establish a *prima facie* case of obviousness, **three basic criteria** must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on applicant's disclosure." (emphasis added)

That is, "reasonable expectation of success" is a separate criterion from the "suggestion or motivation" for the modification of the references.

Secondly, Applicants argued that Hamad et al. did not provide "rapid simultaneous detection" of the bacteria. In the Advisory action, the Examiner stated:

> "However, the claim language recites "a plurality of probes". It is unclear whether or not there are different DNA probes involved in the plurality of probes."

Applicants respectfully submit that the meaning of the Examiner's comments is unclear. Moreover, Applicants submit that the "plurality of probes" in claim 5 clearly refers to different DNA sequences.

The Examiner also states: "The response further argues that Wilding's device was not

capable of analyzing an intestinal bacterial group as recited in claim 5." Applicants are uncertain to which portion of the Response of December 18, 2003, this refers. This may refer to Applicants' contention that "the analysis could not be performed in a **single** device of Wilding's [emphasis added],"which is discussed below.

The Examiner further addressed Applicants' arguments (from page 8 of the Response) that use of Wilding's devices for the stated purpose would require multiple devices, one for each probe, but that this was inconsistent with claim 5. The Examiner stated in the Advisory action:

> "Since the claim language does not define what is the specific position of [sic] a detector. Therefore, the teachings of Hamad et al. in view of Wilding et al. suggest the instant invention."

Applicants are uncertain as to the Examiner's point. The Examiner presumably refers to the claim recitation (before the current amendment) of "said probes are arranged on specific position **on** a detector." However, the Examiner's remarks do not directly rebut Applicants' argument that Wilding does not disclose a single device that can carry out the stated purpose of the claims.

According to the disclosure of Wilding et al., PCR amplification and detection of the amplified DNA fragments are carried out on a substrate. Wilding et al. does disclose that "The substrate may comprise a plurality of detection/reaction chambers to enable the rapid parallel detection of polynucleotides in a mixture." Wilding et al., however, does not disclose how to analyze a plurality of DNA fragments if the plurality of DNA fragments are amplified by one kind of PCR reaction (a reaction caused in one kind of PCR reactive solution).

According to the present invention, a plurality of DNA fragments are amplified by one kind

of PCR reaction and analyzed. This is clearly different from the method disclosed by Wilding et al. The present invention also provides a novel technique of simultaneously identifying and detecting a plurality of DNA fragments by arranging a plurality of probes in parallel.

Hamad et al. discloses that DNA fragments of different bacteria (DNA fragments in a nucleic acid region coding 16SrRNA) can be amplified using the same primer. The disclosure, however, does not mention whether the plurality of DNA fragments from a sample containing a plurality of bacteria can be amplified simultaneously.

The Examiner's statement that "the method according to Hamad et al. was applied to detect a plurality of bacteria since the Sorghum flour contained more than one bacteria" may be true. However, Hamad's detection is carried out by the combination of isolation of bacteria and sequencing of the isolated strains in the 16SrRNA region, which is a time consuming process. It is not possible to apply the method in the technique using a substrate as disclosed by Wilding et al., to Hamad's detection. No combination of Hamad et al. and Wilding et al. would have made it possible to carry out rapid simultaneous detection of a plurality of bacteria.

Reconsideration of the rejection is therefore respectfully requested.

**Claim 6 is rejected under 35 U.S.C. §103(a) as being unpatentable over Hamad et al. (Journal of Applied Microbiology, 1997, Vol. 83, 764-770), in view of Wilding et al. (5,498,392) as applied to claims 4-5, 7-9 and 12-16 above, and further in view of Mullis et al. (4,800,159).** (Office action paragraph no. 9)

The rejection of claim 6 is respectfully traversed, and reconsideration of the rejection is respectfully requested. Applicants have argued above that base claims 4 and 5 are novel and non-obvious over Hamad et al. and Wilding et al. Applicants assert that Mullis et al. does not correct the deficiencies in the *prima facie* case made using Hamad et al. and Wilding et al.

**Claims 12-16 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.** (Office action paragraph no. 11)

The rejection is overcome in part by the amendments to the claims, and is in part traversed.

(a) Claims 12 and 13 have each been amended to be independent, incorporating the limitations of previously canceled claim 11.

(b, first sentence) The Examiner states that the language "a DNA chip in which is arranged a probe on a specific position" is indefinite because "it is unclear whether the DNA chip has an immobilized probe arranged or not." Claim12 has been amended for clarity to change the wording "arranged" to –arranged and immobilized–. Applicant submits that it is clear from the specification and from the general art that in order to be "arranged," that is, located in a specific position on a chip, a probe must be "immobilized." No new matter is therefore added by this amendment.

(b, second sentence) The Examiner states that the language "having a nucleic acid sequence occurring in the genome of the intestinal bacterial group" is indefinite because "it is unclear whether the nucleic acid sequence is comprised by the genome of the intestinal bacteria." This portion of the rejection is respectfully traversed. Applicant is uncertain as to the meaning of the Examiner's

remark, in particular the phrase "comprised by the genome of the intestinal bacteria." Clearly, the nucleic acid sequence of a probe would not generally include (comprise) the entire sequence of the genome of a bacterium. Applicant submits that the present wording is definite. The genome is essentially a long nucleic acid sequence, and the occurrence of a particular nucleic acid sequence as a subsequence of a longer sequence is well understood. The recitation of a particular nucleic acid sequence "occurring in the genome of" an organism or a group of organisms would therefore be well understood by one of skill in the art.

Reconsideration of the rejection is respectfully requested.

In view of the aforementioned amendments and accompanying remarks, claims, as amended, are in condition for allowance, which action, at an early date, is requested.

If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicants' undersigned agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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